similar data on volumetric measurements in water-urea binary mixtures. We find little differences in G_I for protein functional groups in urea and glycine betaine solutions. Comparative analysis reveals that solute-cosolvent interactions are favorable for the glycyl unit and the majority of amino acid side chains in both glycine betaine and urea solutions. These results are consistent with the picture in which the free energy of cavity formation, G_C, is the decisive factor determining the differential stabilizing/destabilizing action of urea and glycine betaine.

2156-Pos Board B142
Examining the Structural Stability of C2B Domain of Synaptotagmin B using Multi-Dimensional NMR Spectroscopy
Rhys Moore.
The non-classical secretion of Human Fibroblast Growth Factor-1 (hFGF-1) is a poorly understood process. hFGF-1 is known to interact with the Ca2+ binding C2B chaperone protein, which escorts FGF-1 to the cytoplasmic side of the cell membrane. The dual-alpha-helical structure of C2B has been well characterized. It not only contains Ca2+ binding sites, but is also binds to Cu2+. Recent studies suggest that Cu2+ shares common binding sites with Ca2+. In the presence of these two metal ions, the 2 binding sites for copper assists in the formation of the hFGF-1/C2B complex, specifically at the amino acid residues Cys-277, Phe-278, Ser-279, Leu-294, Asp-309, Gly-320, Lys-331, Lys-324 and Gly-384. In order to gain a better understanding of this complex reaction, it is desirable to observe the structural stability of the C2B domain of Synaptotagmin B by using multi-dimensional NMR spectroscopy and other biophysical methods. Non-classical release of hFGF-1 presents a promising target for treatment of cardiovascular, oncologic, and inflammatory disorders. Characterization of the three-dimensional solution structure of the complex will provide valuable insights on the design of novel therapeutic principle against hFGF-1-induced pathogenesis.

2157-Pos Board B143
Effect of Ribosomal Surface on Nascent Chain Dynamics
Taisong Zou, Silvia Cavagnero, Banu Ozkan.
Protein synthesis inside the cell is remarkably complex. Various factors like chaperones, enzymatic processing and ribosome can profoundly affect the sequence and nature of the events leading to protein folding in the natural environment. Recent experiments confirm this fact and indicate that there is continuous cross-talk between the ribosome and the translated nascent chain as it emerges out of the exit tunnel. However, the specific ribosomal features that regulate this process at the molecular level are still unclear. Using molecular dynamics simulations, we study the effect of the ribosomal surface by comparing the folding behavior of ribosome-bound with that of ribosome-released nascent chains. Our results show that electrostatic interactions due to the negatively charged ribosomal surface play a role in the regulation of co-translational folding of nascent chain. Polymer theory calculations also support these results.

2158-Pos Board B144
Effect of Confinement on the Folding Dynamics of Amyloid-Beta (21-30) Protein: A Molecular Dynamics Study
Srinivasa Rao Jampani, Luis Cruz.
Confinement is an ubiquitous concept in protein dynamics and studying its effect on protein stability and folding kinetics is necessary to understand protein folding in cellular environments. Confinement easily arises from the crowded in vivo environment that include other proteins and membranes, among others. Effects on the dynamics of the amyloid beta protein of Alzheimer's disease are know to be influenced by it proximity to lipid membranes and other proteins. Here we aim at understanding the relative effects of confinement on the dynamics and folding events of the amyloid beta protein fragment (21-30). For this, we use molecular dynamics in explicit solvent to explore the dynamics of this fragment in differently sized spherical confinement cavities. The different radiuses of the cavities are achieved by dividing the solvent into six different layers of immobile atoms. Starting from a simulation in bulk, each subsequent simulation considers one additional layer of confinement. In this way, the system is slowly taken from bulk to the more confined space. Specifically, starting from a size of 24Å we decrease the radius of the confining spherical cavity to a minimum size of 14 Å. We measure the change in the free energy of the stretched conformation of the amyloid beta (21-30) by varying the confined cavity size. In addition, we study how this confinement affects the stability of pre-formed beta-hairpin conformations by examining possible conformational changes as a function of time along with the lifetimes of these beta hairpin conformations relative to lifetimes observed in the bulk. Lastly, we present results on mutations of the amyloid beta peptide (21-30) that include the Dutch [Glu22Gln], Arctic [Glu22Gly] and Iowa [Asp23Asn] mutations.

2159-Pos Board B145
The Effects of Hofmeister Salts on the Cytochrome c Folding Pathway in Solution and within Sol-Gel Glasses
Jamie L. Odden, **Eric S. Peterson**.
The ferric cytochrome *c* (Cyt *c*) (un)folding mechanism in the presence of steric constraints and altered solvating water structure is examined. Sol-gel encapsulation was used to constrain the protein to a volume slightly larger than the native state. Hofmeister salts were added to alter water order. UV/VIS absorption spectroscopy and a basis spectra fitting analysis were used to determine the populations of species present along the folding pathway. These species can be differentiated by their axial heme ligands. Four species exist in solution: the native HM state (His18/Met80), the partially folded HW (His18/water) and HH (His18/His33) intermediates, and the 5C (water) unfolded state. An additional unfolded state found only within the sol-gel contains an unligated four-coordinate heme sequestered from aqueous solution. In solution, the native HM state unfolds primarily into the HH state, while unfolding within the gel produces comparable amounts of the HH, HW, and four-coordinate states. This indicates that the steric constraints within the gel pores hinder some backbone motions. Four anions (HPO_4^{-2}, $H_2PO_4^{-1}$, SO_4^{-2} and Cl^{-1}) and three cations (Gdn^{+1}, K^{+1}, and NH_4^{+1}) that lie within the Hofmeister series were utilized. Gdn^{+1} lies at one end of the series and promotes unfolding of the protein. Presence of an additional ion can counter the denaturing effects of the Gdn^{+1} to an extent dependant on its proximity to Gdn^{+1} in the series. Both the (un)folding kinetics and the accessible conformations were found to depend on the identity of ions present. A model discussing changes in protein stability as a function of water order and the hydrophobic effect is used to interpret these results. Water order depends on the degree of confinement in the gel pores and the properties of the ions present.

2160-Pos Board B146
Resolving Stability Contributions in the Consensus Tetratricopeptide Repeat
Jacob D. Marold, Thuy P. Dao, Ananya Majumdar, Doug Barrick.
Repeat proteins are constructed from linear arrays of a common structural unit. The physical characteristics that describe the resulting structure depend on the sequence composition of the repeating unit, the number of repeats, and the architectural arrangement of the units with respect to each other[1].
The tetratricopeptide repeat is 34 amino acids in length, and consists of a pair of anti-parallel "A" and "B" α-helices. Regan and coworkers have designed a consensus TPR (cTPR) sequence and characterized the thermodynamic stability and kinetics of folding of a series of cTPRs (1-10 repeats) with a "solubilizing" C-terminal "S" helix[2,3,4]. Their stability data were fit using a homopolymeric model in which the A, B, and S helices were treated as energetically equivalent, although there are significant differences in sequence and packing between the A and B helices. Because the A:B helix ratio was the same in all constructs studied, the homopolymeric model was sufficient to model the thermodynamics of unfolding, despite potential intrinsic energy differences between the different helices. Furthermore, the energy associated with each respective interfacial interaction (A_iB_{i+1}, B_iA_{i+1},B_iS_{i+1}) was not able to be resolved.
To determine whether the A and B helices differ in intrinsic stability (ΔG_A and ΔG_B), and whether interfacial stability (ΔG_{AB} and ΔG_{BA}) values are synonymous, we constructed a series of cTPRs that vary in length, and in the ratio of A to B helices. In addition, we include constructs lacking the C-terminal S-helix. Urea-induced unfolding transitions suggest cooperative folding with a moderate level of nearest-neighbor coupling, as was found by Regan and coworkers. Our results indicate that stability is heterogeneously distributed within cTPR arrays. Although the A and B helices have similar intrinsic stabilities, the energy arising from B_iA_{i+1} interactions contribute more to stability than their A_iB_{i+1} counterparts.

2161-Pos Board B147
Folding Mechanism of a Helix-Turn-Helix Protein from Combined 13C-Edited IR and Mutational Studies
Ginka Buchner, Krista E. Amunson, Jan Kubelka.
Helix-turn-helix motifs are important super-secondary protein structural elements and excellent models for studying the mechanism of protein folding. We have been investigating folding of a *de novo* designed 38-residue helix-turn-helix motif alpha-t-alpha using IR spectroscopy with site-specific ^{13}C isotopic editing. Our preliminary site-specific thermal unfolding data revealed that alpha-t-alpha is most stable near the centers of both alpha-helices, and likely unfolds from the helical termini and the loose turn region. To obtain more detail about the distribution of thermodynamic stabilities along the structure, additional six isotopically labeled proteins were synthesized and investigated using isotopically-edited IR. The new site-specific thermal unfolding data support the proposed folding mechanism, but reveal additional detail about the folding mechanism. The roles of the individual residue-residue stabilizing interactions were further studied by mutations, designed to destabilize the hydrophobic